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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/640,737	08/17/2000	Eva-Maria Mandelkow	28384/36668	5085

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EXAMINER	
CHERNYSHEV, OLGA N	
ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 06/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/640,737	MANDELKOW ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37-42 and 44-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37-42 and 44-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 February 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Claims 37 and 44 have been amended and claims 43 and 50 have been cancelled as requested in the amendment of Paper filed on March 29, 2004. Claims 37-42 and 44-49 are pending in the instant application.

Claims 37-42 and 44-49, in so far as they are directed to a composition comprising a peptide of SEQ ID NO: 1, residues 259-267, are under examination in the instant office action.

2. The Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

4. Applicant's arguments filed on March 29, 2004 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Election/Restrictions

5. On pages 29-30 of the Response Applicant traverses the Election/Restriction requirements as submitted in office action of Paper No. 15. Applicant is advised that arguments to the traversal of the restriction requirement were fully answered before in section 1 of Paper No. 23, in which the restriction requirement was repeated and made final. Therefore, the traversal of the restriction requirement as presented in the Response is considered to be not timely. If Applicant wishes to further review the requirement, an appropriate action would be a petition from requirement for restriction in accordance with 37 CFR 1.144.

Drawings

6. The figures of the instant application remain not in compliance with 37 C.F.R. § 1.84(u) (1) for those reasons of record in section 2 of Paper No. 23. Specifically, the drawings submitted on February 05, 2004 are identified by the number followed by a low case letter, which is not a proper way to present figures.

Furthermore, Figure 1b remains described as containing parts (a) and (b) (see page 23 of the instant specification). However, parts (a) and (b) are not properly identified within Figure 1b.

Applicant is advised to review all the figures of the instant specification for proper presentation and identification.

Double Patenting

7. Applicant is advised that Double Patenting Warning with respect of claims 38, 39, 42, 45, 46 and 49 is maintained in view of the elected invention of a composition comprising a peptide of SEQ ID NO: 1, residues 259-267. See reasons of record in section 6 of Paper No. 23 and reasons of record in section 5 of the instant office action.

New grounds of rejection necessitated by amendment

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 37-42 and 44-49, as amended, are rejected under 35 U.S.C. 103(a) as being unpatentable over Kosik et al. (Proc. Natl. Acad. Sci., USA, 1986, Vol. 83, pp.4044-8) in view of Harlow and Lane, 1988 (Antibodies, Laboratory Manual, Cold Spring Laboratory, pp. 77, 96-97).

Applicant submits that "[a]bsent a finding by the Examiner that the specification or claims lacked a clear indication of what the basic and novel characteristics of the peptide fragments are, "the use of "consisting essentially of" in the present claims should not be construed as "comprising" (middle at page 31 of the Response). This argument has been fully considered but is not deemed to be persuasive. The Examiner agrees that the instant specification

does not present a clear definition of specified materials that supports recitation "consisting essentially of". Therefore, in accordance with MPEP 2111.03, "consisting essentially of" was construed as equivalent to "comprising". Thus, because the instant specification, as filed, clearly lacks indication of what the basic and novel characteristics of the peptide fragments are, and does not provide definition of "consisting essentially of", which would exclude "comprising" language with regards to the amino acid sequence of tau protein, the claims were construed as reciting "comprising" tau protein.

Applicant further submits that claims 37-42 and 44-49, as amended, "recite that the peptide is conjugated to a carrier protein. Neither Kosik nor Vooheis describe conjugation of tau peptide to a carrier protein. Thus, Neither Kosik nor Vooheis anticipate the currently pending claims" (bottom at page 31 of the Response). This argument has been fully considered and, in view of the amendment, rejection under 35 U.S.C. 103(a) is as follows.

On page 18 of the instant specification, it is stated "The methods for obtaining said antibodies are well known in the art; thus, the generation of polyclonal or monoclonal antibodies may be conducted using standard methods (see, e.g., Harlow and Lane, ibid.)". The reference book by Harlow and Lane, "Antibodies. A laboratory manual", teaches standard methods for generation of antibodies. Specifically, information regarding carrier protein that can be used for coupling with peptides is described on page 77, and different adjuvants, nonspecific stimulators of the immune response, are disclosed on page 96-97.

The immunogenic composition of tau protein disclosed by Kosik et al. was prepared from Alzheimer's brain similarly to the protocol disclosed in the instant specification (page 45-46). Thus, Kosik et al. disclose immunogenic composition comprising a peptide comprising amino

acid sequence of tau peptide. Kosik et al. do not expressly disclose conjugation of tau peptide to a carrier molecule. Laboratory Manual by Harlow and Lane discloses coupling (conjugation) of a peptide with a carrier protein for better immunogenic results. At the time the invention was made, it would have been *prima facie* obvious to a person of ordinary skill in the art to conjugate tau peptide of Kosik et al. to a carrier molecule, as disclosed in Harlow et al. According to Applicant's own statement and reference to a laboratory manual, methods of production of antibodies to specific proteins are well known in the art. One skilled in the art would have been motivated to do this because of well-known benefits of conjugation of immunogenic peptides to enhance an immune response.

11. Claims 37-42 and 44-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vooheis, US Patent No.5,492,812, 1996, filed on 08/01/1991 in view of Harlow and Lane, 1988.

Claims 37-42 and 44-49 are directed to an immunogenic composition comprising a peptide comprising an amino acid sequence of tau protein and methods of producing an antibody to tau protein. Vooheis discloses a sequence (SEQ ID NO: 2), which has 100% identity to a fragment 259-267 of SEQ ID NO: 1 of the instant application. Vooheis also discloses the purification of tau-proteins from human brains of patients who died with Alzheimer's disease (columns 7-8) and methods of generation of antibodies that define tau-peptides (columns 12 and 13). Vooheis does not expressly disclose conjugation of tau peptide to a carrier molecule. Laboratory Manual by Harlow and Lane discloses coupling (conjugation) of a peptide with a carrier protein for better immunogenic results. At the time the invention was made, it would have been *prima facie* obvious to a person of ordinary skill in the art to conjugate tau peptide of Vooheis to a carrier molecule, as disclosed in Harlow et al. One skilled in the art would have

been motivated to do this because of well-known benefits of conjugation of immunogenic peptides to enhance an immune response. See also reasons of record in section 10 of the instant office action.

Conclusion

12. No claim is allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (571) 272-0870. The examiner can normally be reached on Monday to Friday 9 AM to 5 PM ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)0. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 872-9306. If this number is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (571) 273-0870. Official papers should NOT be faxed to (571) 273-0870.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Olga N. Chernyshev, Ph.D.

OLGA N. CHERNYSHEV, PH.D.
PATENT EXAMINER